UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

July 28, 2016

MEMORANDUM

Subject: Acute Toxicity Review for EPA File Symbol 91413-E
Data Package 426280
Product Name: Nouvex Technical Antimicrobial Polymer

From: Wallace Powell, Biologist
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Product Science Branch
Antimicrobials Division (7510P)

Through: For Karen Hicks, Team Leader
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To: Eric Miederhoff, PM 31/Cletis Mixon
Regulatory Management Branch I
Antimicrobials Division (7510P)

Applicant: Poly Group LLC

FORMULATION FROM PROPOSED LABEL:

Active Ingredient:	% by weight
Pyridine, 4-ethenyl-, polymer with alpha-(2-methyl-1-oxo-2-propen-1-yl)-omega-methoxypoly(oxy-1,2-ethanediyl), compd. with 1-bromohexane (EPA PC Code 012309)	99.0
Other Ingredient(s):	1.0
Total:	100.0

BACKGROUND

In support of registration for the subject product, Nouvex Technical Antimicrobial Polymer, the applicant has submitted studies for acute oral, acute dermal, and acute inhalation toxicity, eye and dermal irritation, and dermal sensitization.

RECOMMENDATION

The six submitted studies are acceptable. A review of each study is attached to this memorandum. The MRIDs and the assigned Acute Toxicity Categories are listed in the Summary table below.

Summary

The acute toxicity profile of Nouvex Technical Antimicrobial Polymer is currently:

Study	MRID	Toxicity Category	Status
Acute Oral Toxicity	49553203	IV	Acceptable
Acute Dermal Toxicity	49553204	IV	Acceptable
Acute Inhalation Toxicity	49553205	IV	Acceptable
Primary Eye Irritation	49553206	III	Acceptable
Primary Dermal Irritation	49553207	IV	Acceptable
Dermal Sensitization	49553208	Non-sensitizer	Acceptable

Product Labeling

In accordance with the Agency's *Label Review Manual* (www.epa.gov/oppfead1/labeling/lrm), the First Aid statements and human-hazard Precautionary Statements in the submitted labeling (file name: 091413-00001.20150128.pdf) are acceptable.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (OPPTS 870.1100)

Product Manager: 31
MRID No.: 49553203

Reviewer: W. Powell
Study Completion Date: 10/31/2013
Report No.: 37123

Testing Laboratory: Product Safety Labs
Author: Jennifer Durando

Quality Assurance (40 CFR §160): Included

Test Material: Pyridine, 4-ethenyl-, polymer with alpha-(2-methyl-1-oxo-2-propen-1-yl)-2-propen-1-yl)-omega-methoxypoly(oxy-1,2-ethanediyl), compd. with 1-bromohexane
A powder

Dosage: 5,000 mg/kg
Applied as a 25% w/w mixture in corn oil

Species: Rat, Sprague-Dawley derived
Sex: 3 Females
Age: 10-11 weeks
Weight: 186-194 grams
Source: Harlan Laboratories, Inc.

Method: Up-and-Down Procedure. Limit test.

Summary:

1. **Estimated LD_{50}**: > 5,000 mg/kg
2. **Toxicity Category**: IV
3. **Classification**: Acceptable

Deviations from Guideline 870.1100: None noted.

Results:

With administration of the test substance by oral gavage at a dose of 5,000 mg per kg body weight to female rats in a stepwise manner (first one rat and then, upon survival, two other rats), all three rats survived the 14-day observation period. The results indicate an acute oral LD_{50} of greater than 5,000 mg/kg. In-life clinical signs were limited to hypoactivity, soft feces, diarrhea, reduced fecal volume, ano-genital staining; all animals recovered by Day 5 and appeared active and healthy for the remainder of the study. All animals gained body weight during the observation period. Post-mortem necropsy revealed no gross abnormalities.

Reported Mortality

Dosing Sequence	Dose Level (mg/kg)	Short-Term Outcome	Long-Term Outcome
1	5,000	O	O
2	5,000	O	O
3	5,000	O	O

O = Survival

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (OPPTS 870.1200)

Product Manager: 31
MRID No.: 49553204

Reviewer: W. Powell
Study Completion Date: 10/2/2013
Report No.: 37124

Testing Laboratory: Product Safety Labs
Author: Jennifer Durando

Quality Assurance (40 CFR §160): Included

Test Material: Pyridine, 4-ethenyl-, polymer with alpha-(2-methyl-1-oxo-2-propen-1-yl)-2-propen-1-yl)-omega-methoxypoly(oxy-1,2-ethanediyl), compd. with 1-bromohexane
A powder

Dosage: 5,000 mg/kg
Applied as a dry paste, 65% w/w mixture in distilled water

Species: Rat, Sprague-Dawley derived
Sex: 5 Males and 5 Females
Age: 9-10 weeks
Weight: Males 270-284 grams, Females 193-214 grams
Source: Harlan Laboratories, Inc.

Summary:

1. **Estimated LD_{50}**: > 5,000 mg/kg
2. **Toxicity Category**: IV
3. **Classification**: Acceptable

Deviations from Guideline 870.1200: None noted.

Results:

Dermal application of the test substance at a dose of 5,000 mg per kg body weight to male and female rats produced no mortality during the 14-day observation period. The results indicate that the dermal LD_{50} of the sample was greater than 5,000 mg/kg in male and female rats. No in-life clinical signs were found. Necropsy revealed no gross abnormalities. All animals gained body weight during the observation period, though one female lost body weight between Days 7 and 14.

Reported Mortality

Dose Level (mg/kg)	Number Dead / Number Tested		
	Males	Females	Combined
5,000	0 / 5	0 / 5	0 / 10

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (OPPTS 870.1300)

Product Manager: 31
MRID No.: 49553205

Reviewer: W. Powell
Study Completion Date: 10/2/2013
Report No.: 37125

Testing Laboratory: Product Safety Labs
Author: Jennifer Durando

Quality Assurance (40 CFR §160): Included

Test Material: Pyridine, 4-ethenyl-, polymer with alpha-(2-methyl-1-oxo-2-propen-1-yl)-2-propen-1-yl)-omega-methoxypoly(oxy-1,2-ethanediyl), compd. with 1-bromohexane
Test Material, a powder, was applied aerosolized, unground.

Concentration: Gravimetric – 2.08 mg/L
Nominal – 14.60 mg/L

Chamber Type: Nose-only

Species: Rat, Sprague-Dawley derived
Sex: 5 Males and 5 Females
Age: 8-9 weeks
Weight: Males 230-256 grams, Females 175-192 grams
Source: Harlan Laboratories, Inc.

Summary:

1. **Estimated LC_{50}**: > 2.08 mg/L
2. **Toxicity Category**: IV
3. **Classification**: Acceptable

Deviations from Guideline 870.1300: None noted.

Results:

Following a 4-hour exposure, 1 of 5 males, and 0 of 5 females, died during the 14-day observation period. The median lethal concentration, then, is estimated to be greater than 2.08 mg/L in male and female rats. Clinical signs following exposure consisted of abnormal respiration and hypoactivity. All animals recovered from these symptoms by Day 4 and appeared active and healthy for the remainder of the study. Although all surviving animals lost body weight by Day 1, they all gained body weight during the study. Post-mortem necropsy results noted were limited to discolored lungs and liver in the one decedent animal.

Reported Mortality

Exposure Concentration (mg/L)	Number of deaths / number tested		
	Males	Females	Combined
2.08	1 / 5	0 / 5	0 / 10

Chamber Atmosphere

Exposure Conc. (mg/L)	MMAD (µm)	GSD	% of Particles < 4.7 µm
2.08	2.98	2.19	74.1

Chamber Environment

Exposure Level (mg/L)	2.08
Chamber Volume (L)	28
Total Airflow Rate (Lpm)	70.0
Temperature (°C)	23
Relative Humidity (%)	61-65

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (OPPTS 870.2400)

Product Manager: 31
MRID No.: 49553206

Reviewer: W. Powell
Study Completion Date: 10/29/2013
Report No.: 37126

Testing Laboratory: Product Safety Labs
Author: Jennifer Durando

Quality Assurance (40 CFR §160): Included

Test Material: Pyridine, 4-ethenyl-, polymer with alpha-(2-methyl-1-oxo-2-propen-1-yl)-2-propen-1-yl)-omega-methoxypoly(oxy-1,2-ethanediyl), compd. with 1-bromohexane
Dosage: 0.1 mL (0.05 g)

Species: Rabbit, New Zealand albino
Sex: 6 Females
Age: Young adult (not further specified)
Weight: Not specified
Source: Robinson Services, Inc.

Summary:

1. **Toxicity Category**: III
2. **Classification**: Acceptable

Deviations from Guideline 870.2400: None noted.

Note: The test eyes of three of the test animals were rinsed, following application of fluorescein dye but *prior* to application of test substance. The test eyes of three other test animals were not rinsed.

Results:

'Positive' effects − corneal opacity, iritis, and 'positive' conjunctival irritation − were absent in 5 of the 6 tested eyes.

'Positive' effects were observed in one test animal, which was in the Unrinsed group. These effects cleared between Day 4 and Day 7. These effects consisted of corneal opacity form 1 Hour through Day 4, iritis from 24 Hours through Day 4, conjunctival redness from 24 Hours through 72 Hours, and conjunctival swelling at 24 Hours.

Incidence of Irritation – Unrinsed Eyes

Time Post-Instillation	No. of Animals Testing "Positive" / No. of Animals Tested			
	Corneal Opacity	Iritis	Conjunctiva	
			Redness	Chemosis
1 hour	1 / 3	0 / 3	0 / 3	0 / 3
24 hours	1 / 3	1 / 3	1 / 3	1 / 3
48 hours	1 / 3	1 / 3	1 / 3	0 / 3
72 hours	1 / 3	1 / 3	1 / 3	0 / 3
Day 4	1 / 3	1 / 3	0 / 3	0 / 3
Day 7	0 / 3	0 / 3	0 / 3	0 / 3

Incidence of Irritation – Rinsed* Eyes

Time Post-Instillation	No. of Animals Testing "Positive" / No. of Animals Tested			
	Corneal Opacity	Iritis	Conjunctiva	
			Redness	Chemosis
1 hour	0 / 3	0 / 3	0 / 3	0 / 3
24 hours	0 / 3	0 / 3	0 / 3	0 / 3
48 hours	0 / 3	0 / 3	0 / 3	0 / 3
72 hours	0 / 3	0 / 3	0 / 3	0 / 3
Day 4	0 / 3	0 / 3	0 / 3	0 / 3
Day 7	0 / 3	0 / 3	0 / 3	0 / 3

*Rinsed following application of fluorescein dye but prior to application of test substance

DATA REVIEW FOR ACUTE DERMAL IRRITATION TESTING (OPPTS 870.2500)

Product Manager: 31
MRID No.: 49553207

Reviewer: W. Powell
Study Completion Date: 9/23/2013
Report No.: 37127

Testing Laboratory: Product Safety Labs
Author: Jennifer Durando

Quality Assurance (40 CFR §160): Included

Test Material: Pyridine, 4-ethenyl-, polymer with alpha-(2-methyl-1-oxo-2-propen-1-yl)-2-propen-1-yl)-omega-methoxypoly(oxy-1,2-ethanediyl), compd. with 1-bromohexane
A powder

Dosage: 0.5 g of the test substance, 65% w/w mixture in distilled water. (i.e., 0.77 g total, as a dry paste)

Species: Rabbit, New Zealand albino
Sex: 3 Males
Age: Young adult (not further specified)
Weight: Not specified
Source: Robinson Services, Inc.

Summary:

1. **Toxicity Category**: IV
2. **Classification**: Acceptable

Deviations from Guideline 870.2500: None noted.

Results:

Following a four-hour exposure in three rabbits, no signs of dermal irritation were observed at the test sites of any treated animal during the 72 hour observation period.

Individual Dermal Irritation Scores following the four-hour exposure

Animal No.	Sex	Erythema / Edema			
		Time After Patch Removal			
		30-60 min	24 hrs	48 hrs	72 hrs
3501	F	0 / 0	0 / 0	0 / 0	0 / 0
3502	F	0 / 0	0 / 0	0 / 0	0 / 0
3503	F	0 / 0	0 / 0	0 / 0	0 / 0

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (OPPTS 870.2600)

Product Manager: 31
MRID No.: 49553208

Reviewer: W. Powell
Study Completion Date: 10/25/2013
Report No.: 37128

Testing Laboratory: Product Safety Labs
Author: Jennifer Durando

Quality Assurance (40 CFR §160): Included

Test Material: Pyridine, 4-ethenyl-, polymer with alpha-(2-methyl-1-oxo-2-propen-1-yl)-2-propen-1-yl)-omega-methoxypoly(oxy-1,2-ethanediyl), compd. with 1-bromohexane
A powder

Positive Control Material: alpha-Hexylcinnamaldehyde (97.1%)

Species: Mouse, CBA/J, Female
Weight: 17.3-22.3 g (Test and Control groups)
Age: 9-10 weeks (Test Substance and Control groups), 9-10 weeks (Preliminary animals)
Source: Jackson Labs

Method: Local Lymph Node Assay (LLNA)

Summary:

1. The test material did **not** appear to be a contact sensitizer.
2. **Classification:** Acceptable

Deviations from Guideline 870.2600: None noted.

Results:

Stimulation Index (SI) for each Test Substance group and for Positive Control group, was derived by dividing the average net DPM of each group by the average net DPM of the Vehicle Control group, where "net DPM" is measured DPM less background DPM.

Animal Group	Dose Preparation	Average Net DPM	Number of Mice	SI
Vehicle Control	1% Pluronic® L92 w/w in distilled water	715.96	5	—
Positive Control	25% HCA (97.1%) in 1% Pluronic® L92 w/w in distilled water	3954.86	5	5.52
2.5% Test Substance	2.5% test substance in 1% Pluronic® L92 w/w in distilled water	666.21	5	0.93
5% Test Substance	5% test substance in 1% Pluronic® L92 w/w in distilled water	877.74	5	1.23
10% Test Substance	10% test substance in 1% Pluronic® L92 w/w in distilled water	605.39	5	0.85

An SI of 3.0 or greater was not observed in any of the Test Substance groups – thus indicating that the test material was negative for dermal sensitization. The Positive Control group tested positive, as appropriate.

Note: No erythema or edema were found at the test sites in any of the Test Substance groups or the Vehicle Control group.